UNITED STATE EPARTMENT OF COMMERCE
**Patent and Trademark Offic**
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
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| 08/819,669 | 03/17/97 | BOON | LUD-5253.5-D |

EXAMINER: T

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HM12/0328

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | 37 |

1644

**DATE MAILED:** 03/28/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/13/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☑ Claim(s) 173, 174, 176, 179, 181, 182 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☑ Claim(s) 176, 182 is/are allowed.
☑ Claim(s) 173, 174, 179, 181 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

**--SEE OFFICE ACTION ON THE FOLLOWING PAGES--**

## DETAILED ACTION

1. Applicant's amendment, 11/13/00 (Paper No. 35), has been entered.
Claim 176 has been amended.

Claims 173, 174, 176, 179, 181 and 182 are pending.

Claims 1-172, 175, 177, 178 and 180 have been canceled previously.

2. Again applicant's comments on previous interviews and communications are acknowledged.

Again, the current examiner cannot comment on or determine whether the Interview Summary held on 12/23/98 was accurate or not; given that the current examiner was not present at that Interview.

Again, it appears that prosecution has taken into account and has proceeded beyond the specific points raised and requested on pages 2-3 of applicant's amendment, filed 2/5/99 (Paper No. 19.

Again, it appeared that applicant's concerns were addressed at this subsequent Interview and that all agreed to further prosecute the instant application and claims.

Again, the examiner apologizes for any misunderstanding or inconvenience to applicant.

Again, as pointed out previously, this Office Action addresses the current claimed invention and takes into account the prosecution history set forth in the instant file application

3. Again, while it is acknowledged that both "BALB/C" and "BALB/c" are used in the literature to describe this mouse strain; applicant is reminded that "BALB/c" is the proper designation of this mouse strain (see pages 27-28).

4. Applicant is reminded of the following.
The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.
The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).
The reference to USSN 07/764,364 in the oath appears in error, as this application issued as U.S. Patent No. 5,327,252 directed to a print apparatus.
Application Number 764,364 has the last "4" crossed out and "PCT/US92/04354 / 22 May 1992" has been crossed out.

Although applicant's amendment, 11/13/00 (Paper No. 35), did not comment on the defective oath; applicant's amendment, filed 6/30/00 ({Paper No. 29); applicant will address the defective oath upon allowance.

5. Upon reconsideration of applicant's amended claims, filed, 11/13/00 (Paper No. 35); the previous rejection of claims 176 and 182 under 35 U.S.C. § 112, second paragraph, with respect to the recitation of "stringent conditions" has been withdrawn.

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that this is a written description rejection rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

Claims 173, 174, 179 and 181 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Tumor antigen precursors are processed to form the presentation of tumor rejection antigens (page 6 of the specification), including but not limited to those most characteristic of a particular tumor (page 8 of the specification)

While the peptide consisting of SEQ ID NO: 26 from Exon 3 of MAGE-1 can be used to confer sensitivity to anti-E cytotoxic T cells. (See Example 34, pages 34-35 of the instant specification); a tumor antigen precursor is a much larger molecule than that defined by 9-mer.

It appears that the claimed tumor antigen precursor is drawn to the E antigen precursor gene which is set forth in SEQ ID NO: 7 or SEQ ID NO: 8 (see Example 20-26, pages 37-6 of the specification).

For example, the instant specification discloses in Example 21 (page 40) that the tumor antigen precursor E antigen is identified by either a 2.4 kb genomic segment of 1.8 kb mRNA segment and that gene extends over about 4.5 kb as shown in Figure 8

Also, the specification discloses in Example 23 (pages 41-46 ) that MAGE refers to a family of tumor rejection antigen precursors molecules which share a certain degree of homology. Example 25 (page 43) acknowledges that genes encoding MAGE-1,-2-3 cross hybridized to a considerable extent.

Further it is noted that Ding et al. (Biochem. Biophys. Res. Commun. 202: 549-555, 1994) discloses that homologous MAGE-1 can be polymorphic (see entire document, particularly page 551, paragraph 1).

The instant claims are drawn to a tumor rejection antigen precursor comprising the 9-mer peptide SEQ ID NO: 26.

A 9-mer peptide does not provide sufficient written description provision of 35 USC 112, first paragraph of a tumor rejection antigen precursor.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed tumor antigen precursor and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences.

The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Here, the specification does not provide sufficient written description of a tumor antigen precursor based upon the limited disclosure/recitation of a much smaller tumor antigen (versus tumor antigen precursor). There is insufficient written description of the structure / sequences that flank the 9-mer SEQ ID NO: 26 that define a MAGE-1 tumor antigen precursor and, in turn, provide the appropriate structural and functional attributes of a MAGE-1 tumor antigen precursor.

Further, given the polymorphism and homology of MAGE tumor antigen precursors; there is insufficient written description of the alternative forms of a tumor antigen precursor comprising the limited 9-mer SEQ ID NO: 9.

Therefore, there is insufficient written description for the tumor antigen precursor based upon the limited recitation of the 9-mer SEQ ID NO: 26 under the written description provision of 35 USC 112, first paragraph.

8. Claims 173, 174, 179 and 181 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a MAGE-1 tumor antigen precursor encoded by SEQ ID NO: 8 or nucleic acid sequences that hybridize to said SEQ ID NO: 8; does not reasonably provide enablement for any "tumor antigen precursor comprising SEQ ID NO: 26.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

While the peptide consisting of SEQ ID NO: 26 from Exon 3 of MAGE-1 can be used to confer sensitivity to anti-E cytotoxic T cells. (See Example 34, pages 34-35 of the instant specification); a tumor antigen precursor is a much larger molecule than that defined by 9-mer.

Applicant has not provided sufficient biochemical information (e.g. nucleic acid or amino acid sequence) that distinctly identifies tumor antigen precursors comprising the 9-mer SEQ ID NO: 26, encompassed by the claimed invention.

While the recitation of "tumor antigen precursor" may have some notion of the properties of the claimed molecule(s), claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use the "tumor antigen precursors", commensurate in scope with the claimed invention.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

As pointed out above in Section 7; there is acknowledged polymorphism and homology among MAGE tumor antigens, including MAGE-1.

There is insufficient guidance and direction as to how to make and use tumor antigen precursors comprising SEQ ID NO: 26, other than that encompassed by a larger sequence (e.g., SEQ D NO: 8) or some other set of structural or functional attributes that define a tumor antigen precursor rather than relying upon the recitation of the 9-mer SEQ ID NO: 26 only.

Tumor antigen precursors are processed to form the presentation of tumor rejection antigens (page 6 of the specification), including but not limited to those most characteristic of a particular tumor (page 8 of the specification)

A person of skill in the art is not enabled to make and use a MAGE-1 tumor antigen precursors, which can be processed to form the presentation of tumor rejection antigen such as SEQ ID NO: 26 and be characteristic of a particular tumor. The skilled artisan would not predict that all that is required for a tumor antigen precursor is the 9-mer SEQ ID NO: 26. A skilled artisan would expect that other structural and functional attributes would be required to provide a MAGE-1 tumor antigen precursor its ability to be processed to form a tumor rejection antigen characteristic of a particular tumor.

For example, a person of skill in the art could not predict which particular amino acid sequences in addition to SEQ ID NO: 26 would be sufficient to confer a MAGE-1 tumor antigen precursor with the ability to be processed to form a tumor rejection antigen characteristic of a particular tumor

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, making and using tumor antigen precursors comprising SEQ ID NO: 26, while providing or maintaining the structural and functional attributes of a MAGE-1 tumor antigen precursor would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

9. Claims 173, 174, 179 and 181 are rejected under 35 U.S.C. 112, first paragraph.

Claims 176 and 182 are allowable over the prior art of record.

U.S. Patent No. 5,843,448 is made of record and is considered pertinent to applicant's disclosure.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
March 26, 2001